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AdvaMed
Advanced Medical Technology Association

November 14, 2005

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Docket 2005D-0348; Draft Guidance for Industry and FDA Staff, Procedures for Handling Post-Approval Studies Imposed By PMA Order

Dear Sir/Madam:

Introduction:

AdvaMed, the Advanced Medical Technology Association, submits the following comments on Docket #2005D-0348 "Draft Guidance for Industry and FDA Staff, Procedures for Handling Post-Approval Studies Imposed by PMA Order." Hereafter we will refer to Post-Approval Studies Imposed by PMA Order as CoA (Condition of Approval) studies.

AdvaMed is the world's largest association representing manufacturers of medical devices, diagnostic products, and medical information systems. AdvaMed's more than 1,300 members and subsidiaries manufacture nearly 90 percent of the $80 billion of health care technology products purchased annually in the United States, and more than 50 percent of the $175 billion purchased annually around the world. AdvaMed members range from the largest to the smallest medical technology innovators and companies. More than 70 percent of our members have less than $30 million in domestic sales annually.

Advisory Panel Presentation

AdvaMed acknowledges the need for FDA to seek the advice of an Advisory Panel when considering the initiation or progress of post-approval studies. We also recognize that it may be appropriate to update the Advisory Panel on the status and outcomes of any device that was reviewed by an Advisory Panel during premarket evaluation.

The draft guidance appears to suggest that sponsors will update the Advisory Panel only on study **status**, whereas the Agency will present **analysis and evaluation** of the study to date. We therefore strongly suggest that this section be rewritten to clearly state that sponsors will

be invited to present their analysis and evaluation of study data to date before the Advisory Panel. AdvaMed strongly encourages FDA to work collaboratively with sponsors to develop a clear and balances presentation. Adequate time (at least 30 days) should be available to prepare Advisory Panel presentations.

Least Burdensome

The Post-Approval Study Status reporting interval should be stated in the Approval Order and should be determined based on individual device characteristics, the target population, and an appropriate risk analysis. The 6-month reporting minimum reporting interval should be removed from the guidance. The establishment of a fixed minimum reporting interval is not a "least burdensome" approach.

The Post-Approval Study Status and Final Report should be submitted in the PMA Periodic (Annual Report) Report since the majority of the information is duplicative. To facilitate the dissemination and review of the Study Status and Final Report, they should be submitted as separate sections. This would allow for a least burdensome approach for both the Sponsor and FDA since only one report would have to be submitted and tracked.

Study Termination

AdvaMed recommends that this guidance take into consideration the possibility that some studies will experience external influences that will affect patient enrollment and completion of a CoA study as originally planned. Such influences may include the subsequent availability of pharmaceutical therapies, different medical device technologies, or the market release of another generation of the original device. Other factors, outside the control of sponsors, such as the inability of hospitals to obtain 3rd party reimbursement or insurance coverage, due to the perception that Condition of Approval study means that the device is *conditionally* approved, can also interfere with study completion.

In such situations, the sponsor should be able to work with the FDA to arrange an appropriate change or closure of the study. The guidance should provide a procedure for making appropriate changes to a study and should not consider such situations to be non-compliance on the part of the sponsor.

Unforeseen product life cycle and market forces may make study completion impossible within the terms of the original study commitment. The guidance should recognize this possibility and state the procedure for terminating a study due to inadequate enrollment of patients, physicians, or participating hospitals.

Protocol Action

CoA protocols are currently approved by 180-day Supplement. FDA has acknowledged that action on sponsor submitted protocols should require substantially less than 180 days. AdvaMed is proposing a 30-day action cycle for sponsor submitted protocols. Furthermore, although CoA Protocols are submitted via PMA 180-day Supplement they are not subject to user fees. The guidance should refer sponsors to Section VI of “Guidance for Industry and

FDA: User Fees and Refunds for Premarket Approval Applications" http://www.fda.gov/cdrh/mdufma/guidance/1224.html. Furthermore, we suggest that the guidance direct the sponsor to label the 180-day Supplement submitted for protocol approval: "Post-approval Study Protocol – Not Subject to User Fee."

Clarification

The guidance should be consistent with the use of terms throughout the document. For example, the term "Interim Study Status Reports" is defined on page 6 of the document. However, it is not consistently used throughout the document as described below:

- On page 7, it is referred to as an **interim** report in the definition of "Delayed."
- On page 8, it is referred to as a **"Post-Approval Study Status Report"** in the headline of what should be included in the report.
- On page 9, it is referred to as a "**Postmarket Study Interim Report"** in Section II, Type of Submissions.
- On page 10, it is referred to as an "Interim Report" in the second bullet at the top of the page; and "interim study report" in Section III Study Information, 8th sub-bullet.
- On page 11, it is referred to as a "**Post-Approval Study Status Reports**" several times.

The guidance should indicate the number of copies and acceptable formats (e.g. paper, PDF) that can be used for submissions. The guidance should clearly state whether approved CoA studies, which are underway, are within the scope of this guidance. FDA should respond to sponsors within 30 days of receipt of a Study Status Report that the report has been received and is complete.

Public Disclosure of Study Status

The guidance should clearly state the expected details for all elements subject to public disclosure on the FDA website. The guidance should state the source of the Commitment Description i.e., will this language be taken directly from the approval letter, or for commitments finalized after approval, from the FDA's letter confirming the commitment? AdvaMed believes that the summary section of the Study Status (page 10, Section III, last bullet) report should be limited to the following.

- unanticipated adverse events
- unanticipated volume of adverse events
- unusual observations

The interpretation of study results is more appropriate for the Final Study Report or in interim reports that are required by the approved study protocol.

AdvaMed wished to bring to your attention two editorial errors. On page 8, the word "studies" is missing in the first sentence between the words "post-approval" and "depends upon." In the middle of page 9 the bullet points starting from "Phone Number (include area code)" to "Contact e-mail address" appear to be superfluous.

Criteria for Condition of Approval Studies

Although this guidance is directed at procedures for handling CoA Studies, AdvaMed wishes to enter into the public record three broad principles which should guide the Agency in establishing the criteria for ordering CoA studies and the design of CoA studies so ordered. The following is based on the "Principles of Condition of Approval Studies" were first presented to FDA in February of this year.

1. A CoA study should be designed to answer only clearly defined questions pertinent to ensuring the continued safety and effectiveness of the approved device.

2. FDA should only require additional data when existing data collection methods (e.g. registry) are not sufficient to ensure continued safety and effectiveness of the approved device.

3. A CoA study should be designed to provide the necessary additional data in the most reasonable fashion, taking into account study center logistics, timeframe, and patient recruitment. Protocol criteria should not be so prescriptive to limit or exclude valuable real-world data.

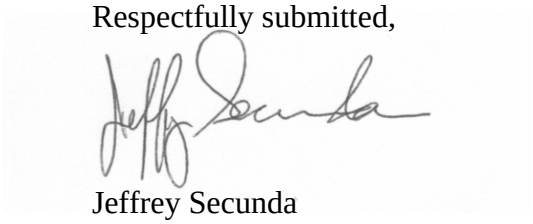
AdvaMed acknowledges that this guidance document, for the most part, is in alignment with the principles which we put forth is the February document.

AdvaMed fully supports FDA's desire to seek agreement on CoA study protocol before imposing post-approval studies as a condition of approval. This approach is both logical and avoids the time and expenses, for FDA and Industry, of submitting a 180-Supplement for protocol approval.

AdvaMed is grateful for this opportunity to commend FDA on this well thought out document, especially in light of its rapid development. The timely development of good guidance documentation helps both the Agency and the Industry develop, evaluate, and approve new medical technology to for the benefit of all Americans and the citizen of the world.

We appreciate the opportunity to share our concerns with FDA and look forward to working with the Agency to address issues related to this important guidance.

Respectfully submitted,



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